REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 16, 20-23, 31 and 32 will be pending in the application subsequent to entry of this Amendment which accompanies a Request for Continued Examination. This Amendment addresses the issue raised in the Official Action of July 3, 2008, a Final Rejection.

The sole issue raised is the inventiveness of all of the then pending claims over the published European patent 0466037 to Rorstad et al in view of U.S. 6,143,883 to Lehmann et al. Previous rejections with these two documents cited individually have been withdrawn and the current rejection is based upon a combination of both documents.

It appears that the Rorstad document (EP '037) is now regarded by the Examiner as the closest prior art. The Rorstad disclosure describes **prevention** of illness and not **treatment** of illness. Claim 1 of the instant application is explicitly limited to the **treatment** of inflammation and/or wound healing in aquatic animals and therefore requires that a wound or inflammation has already occurred.

At the start of the detailed description of the invention section of the Rorstad document, it is stated that the class of yeast glucans described in Rorstad is a very effective prophylactic medicament. It is used to prevent fish illness or to enhance the effect of a vaccine and is not used to treat an existing condition. The prophylactic use of yeast glucans does not at all make it obvious that those glucans could be used to treat conditions, especially wounds once they are manifested. We take all sorts of precautions to prevent disease but very rarely do any precautions which prevent disease actually treat the disease if you get it. It is very important to note therefore that Rorstad fails to consider treatment of any diseases whatsoever.

Wound healing is an aspect of the present invention; *see* for instance page 1, last line, page 3, line 14 and page 4, lines 8 and 22-24 of the description. It is also specifically clamed in claim 16 and new dependent claim 32. Wound healing is far removed from prophylactic treatment. There is no medicament that can be used to prevent wounds occurring as these are caused by a physical trauma. No one considering how to treat a wound would therefore turn to a document such as Rorstad that is describes prevention of unrelated diseases.

Consider next the definition of the glucan -- claim 1 now requires the use of a water soluble glucan. The Examiner appears to take applicant's arguments that M-glucans are not

water soluble as this is explicitly stated in Rorstad on page 6, line 7. The Examiner argues that Rorstad allows for the use of a variety of different glucans but at no point in any passage highlighted by the Examiner is there mention of a water soluble glucan. The Examiner appears to argue that the broad definition of glucans in Rorstad covers water soluble glucans but provides no evidence of that either in the reference itself or any other document.

It is knowing that 1,3/1,4 glucans tend to be water soluble. However, 1,3/1,6 glucans which are the subject of this application tend to be water insoluble. Note therefore that on page 3 of the instant application applicant states that his glucans are obtained from Baker's yeast (*Saccharomyces cerevisiae*) but which are processed to render them soluble. One does not simply extract a water soluble glucan from Baker's yeast, you need to process it.

Note also that the M-glucans in Rorstad are obtained from exactly the same compound, Baker's yeast, but are not treated to make them soluble. There is absolutely no suggestion anywhere in Rorstad that any of the glucans it discusses are treated to make them soluble. There are certainly no disclosures of solubility in terms of a beta-1,3/1,6 glucan as required by claim 16. Moreover, given the preferred embodiment of the Rorstad document is to use an **in**soluble glucan there is absolutely no motivation to manufacture water soluble glucans.

Regarding the mode of administration, applicant has already discussed that the term "aqueous exposure" covers a lot more than water immersion. Applicant also again asks the Examiner to reconsider the point that the aqueous exposure should be read in conjunction with the fact that Rorstad certainly does not disclose water soluble glucans. All of his examples involve injection of the active agent in fish and at no point does the Rorstad disclosure consider whether it is possible to administer an active agent to a fish via water immersion treatment. It would be obvious that injecting the active agent directly into a fish ensures that the fish takes on a certain amount of the active agent. Feeding the fish the active agent also ensures that a certain amount of it is ingested. When you are simply placing the fish in a water bath containing the active agent Rorstad does not make it obvious that a clinical dose of the active agent would be provided to the fish.

It is submitted in fact that Rorstad could not possibly have realized this because injecting a fish with the active agent is a difficult procedure. Fish are inherently slippery and difficult to inject. If Rorstad had realized that he could administer compounds to fish via water immersion

then surely that would have been a preferable route than to inject the fish. Rorstad does not do this because he does not realize that a clinical dose can be administered and/or he does not appreciate that he can use a soluble glucan.

The present inventor is the first person to realize that clinical doses can be administered via water immersion using water soluble glucans. The advantages of this procedure are widespread. It is an easier procedure as you do not need to touch the fish and as applicant has previously highlighted touching fish damages their skins. Using a water bath treatment one can treat a number of fish at the same time. One can treat the whole body surface of a fish at the same time. It is submitted therefore that Rorstad does not in any way disclose the present invention.

Turning then to the Lehmann disclosure, this document does disclose a water soluble glucan. The applicant in no way claims that water soluble glucans are new but this document provides further evidence that at the time of Rorstad (circa 1992) there were no water soluble glucans so Rorstad could not disclose them. The background section of Lehmann mentions that the fact that naturally occurring glucans are insoluble and these are the glucans used by Rorstad.

The M in M-glucans stands for "microparticulate" - they are designed therefore to be insoluble in water.

In fact when Rorstad was written, there were almost certainly no water soluble glucans available. Water soluble compounds are difficult to make (and the subject of major US litigation incidentally).

The M glucan products include a very fine insoluble particulate product dispersed in water. This product was trialed as a therapeutic treatment by addition to water containing fish and invertebrates to investigate its benefits for the management and treatment of wounds and inflammation and no significant benefit was noted. In contrast, the soluble glucans used by addition to the water had an immediate impact noted as a reduction in skin inflammation and a rapid increase in the rate of wound healing. This included the clinical management of eye wounds, where soluble glucans have an immediate topical contact due to their distribution in a soluble state in the animal environment.

Gunar Rorstad was the previous director of Biotec ASA, and the particulate glucans (M-Glucans) they supplied did not work effectively in clinical management of wounds and inflammation via environmental application in aquatic animals.

It is simply not possible for particulate glucans to be taken up across the gill surface. There are no active transport processes for this at this site (unlike the gastrointestinal system, where uptake can occur). Soluble glucans can cross the gill, along with ionic and water flux which forms part of the normal osmoregulatory function of the fish. This equally applies to the skin in fish , which has special properties allowing water flux unlike mammals for example which have relatively impermeable skin, which would not allow such flux to occur. It is therefore the case that glucans of suitable molecular weight, can cross the gills and/or skin in aquatic animals and can therefore exert a significant systemic effect. This of course is also synergistic with the topical availability to the entire external surface of the animal, and the gastrointestinal tract in species which consume the water. The clinical effects therefore can be of greater benefit compared to particulate forms applied orally or topically or as environmental dispersions.

The Examiner dismisses applicant's arguments regarding the nature of the animals to be treated in this document because fish and crustaceans are mentioned in column 4, line 62. To rely on a combination of documents however, anyone reading Rorstad must turn also to Lehmann for further inspiration. Given that Rorstad is very definitely in the field of fish treatment and Lehmann is very definitely in the field of treating mammals (their examples are on human blood cells) this combination appears obscure. Mammals are all related creatures and drugs that can treat conditions in human beings are often found valuable to treat conditions in other mammals. Fish and crustaceans have physiology utterly different than a mammal. There is no way of linking the activity of a pharmaceutical for a mammal to a fish.

Applicant routinely test new drugs on mammals, starting with mice moving on to dogs and primates. Applicant never uses fish or crustaceans as a human model! Throughout the document from the title to column 8, line 1 the animals to be treated are specified as mammals. The Examiner would have the skilled man ignore all this disclosure and pick up only on the disclosure of two words which contradict every other disclosure in the document.

Even if the skilled man can somehow work out that this document does indeed relate to fish there is still no disclosure of water immersion treatment. There is absolutely no suggestion in Lehmann that the clinical dose of particular compound can be administered to a fish via its immersion in a water bath containing the compound. Lehmann discloses conventional modes of administration to a mammal such as orally or administration or as a topical cream, lotion, salve or ointment. Applicant is not aware of any mammalian treatment for wound healing or inflammation which involves water immersion. Given the vast majority of mammals would drown this is perhaps unsurprising. Note of course, that it is not possible simply to "dip" the mammal in a water bath (like sheep dip). That would not give the necessary exposure to the active agent which is achieved when a fish is exposed to the treatment. Applicant has already provided photographic evidence of a fish treated by water soluble glucans in the last response and the healing period is weeks not 10 seconds.

Neither Lehmann or Rorstad teach that a clinical dose of a compound can be administered by water immersion using a water soluble glucan to a fish or crustacean.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration and allowance are solicited.

Respectfully submitted,

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